3   NON-INVASIVE SPECTROSCOPY OF MAMMALIAN TISSUES

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5

6 FIELD OF THE INVENTION

7   This invention relates to the non-invasive, spectrometric,

8 assessment of hemoglobin in the blood of mammalian tissues.

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10 BACKGROUND

11   The assessment of blood in mammalian tissues is important in

12 different scientific disciplines. In medicine, the assessment of blood,

13 and in particular, the assessment of hemoglobin concentration in the

14 blood, is important in the diagnosis and treatment of many diseases

15 and dysfunctions. In forensic science, the assessment of blood is an

16 indication of contusions or bruises of the skin, which are typical

17 consequences of blunt impact trauma. The invention concerns the

18 non-invasive, spectrometric, assessment of hemoglobin concentration

19 in blood in mammals. Two significant applications of this technology

20 are in the diagnosis of anemia, in which hemoglobin concentration is

21 assessed, and in the determination of blunt force trauma, in which

22 hemoglobin degradation and aging is assessed. These two

23 applications are discussed below.

24 A.   Anemia

25   Anemia is often perceived by the general population to be a

26 minor medical condition. However, according to the World Health

27 Organization (WHO), anemia is the single, largest global illness

1   adversely affecting mortality and worker capacity. The United States

2   Department of Health & Human Services deems it a significant public

3   health concern. Of the 16 million people estimated to have anemia in

4   the United States, 78% go undiagnosed. In developing countries where

5   nutritional inadequacies and infectious diseases are more prevalent,

6   the situation is estimated to be even worse.

7   Anemia is a deficiency in the number of healthy red blood cells

8   in an individual's body. This deficiency results in oxygen deficiency in

9   the body's tissues and organ systems. Medically, anemia is defined by

10 the WHO as a hemoglobin concentration below 12 g/dL for females

11 and below 13 g/dL for males. Anemia is well known to the general

12 public to influence physical function by causing fatigue and weakness.

13 It also decreases myocardial function and increases peripheral arterial

14 vasodilation and activation of the sympathetic and reninangiotensin-

15 aldosterone system, which strongly influences the initiation or

16 progression of diseases such as heart failure and renal failure. In

17 addition, anemia affects individuals with other diseases; at least 33%

18 of cancer patients, 65-95% of HIV/AIDS patients, and 70% of

19 rheumatoid arthritis patients also have anemia.

20   Age-related disability and loss in physical function are mounting

21 public health concerns. Loss of physical function endangers the

22 quality of life and independence of many older adults and has

23 significant social and economic repercussions. The prevalence of

24 anemia increases with age and averages about 13% in persons' over 70

25 years of age. A majority of the anemia in aging adults signifies

1   diseases such as cancer and infectious ailments or are due to iron

2   deficiency or malnutrition. Recent studies indicate that anemia in

3   aging adults ins an independent risk factor for decline in physical

4   performance and is associated with higher mortality risks.

5   Yet anemia is severely under-diagnosed. The reasons are two-

6   fold. To determine if a patient is anemic, the physician can either

7   make a visual inspection of the palpebral conjunctiva of the eye socket

8   or take a blood sample and have a cell blood count (CBC) test run.

9   Visual inspection, dependent on the physician's experience and

10 training, is at best only 70% accurate and it has been shown that

11 physicians today are less accurate in diagnosing anemia by visual

12 inspection that in the past. Hung, et al., Evaluation of the Physician's

13 Ability to Recognize the Presence or Absence of Anemia, Fever, and

14 Jaundice, *Academic Emergency Medicine 7: 146-56* (2000). The CBC

15 test is very accurate, but painful and expensive to perform, time-

16 consuming and often not included in a routine examination.

17   Because of the need to assess hemoglobin concentration in a

18 more accurate and effective manner, a number of devices and methods

19 have been proposed. Exemplary are (i) retinal imaging, see United

20 States Patent No. 6, 305,804 entitled Non-Invasive Measurement of

21 Blood Component Using Retinal Imaging, (ii) blood oxygenation

22 monitoring, see United States Patent No. 6,456,862 entitled Method

23 for Non-Invasive Spectrophotometric Blood Oxygenation Monitoring

24 and United States Patent No. 6,149,589 entitled On-Line and Real-

25 Time Spectoreflectometry Measurement of Oxygenation in Patients

1   Eye, (iii) in-vivo imaging of blood, see United States Patent No.

2   6,104,939 entitled Method and Apparatus for Reflected Imaging

3   Analysis, (iv) blood analyzer technology, see United States patent

4   5,791,345 entitled Non-Invasive Blood Analyzer, and (v) image

5   processing of blood vessels, see United States Patent No. 4,998,533

6   entitled Apparatus and Method for In Vivo Analysis of Red and White

7   Blood Cell Indices. None of these proposed solutions has been

8   embraced by health care professionals, predominately because of

9   inconvenience and inaccuracies in the results.

10   United States Patent Application Publication No. 2003/0002772,

11   published January 2, 2003 and entitled Non-Invasive Determination of

12   Blood Components discloses a method for estimating an amount of

13   hemoglobin in bodily fluids from the color of a tissue surface of a

14   subject by taking a digital color image of the surface of the subject

15   and a color reference object, decomposing the images into sub-

16   images of component colors having values corresponding to the pixels

17   of the images, selecting a window of each of the images, and

18   calculating an estimated level of hemoglobin using values associated

19   with the component values corresponding to the windows. Although

20   this approach is rapid, due to the inherent noise in this approach, the

21   accuracy of this method is limited.

22   Accordingly, there is still a significant need in the art for a

23   device that can quickly, accurately and non-invasively measure or

24   assess hemoglobin concentration. Such a device would have many

25   health care applications, such as in routine physical examinations, in

1   emergency rooms, for emergency rescue professionals, during surgery

2   for in-situ measurement of bleeding, for home health care for the

3   chronically ill and aging population, in developing countries lacking

4   medical facilities, in military medical units and in mass casualty

5   situations and triage units, and by oncology, pediatric, obstetric and

6   gynecology, anesthesiology, infectious disease, gastroenterology,

7   cardiology, nephrology, geriatric and urology specialists who deal with

8   anemia on a·regular basis.

9   B.   Forensics

10   Visible contusions or bruises of the skin, the typical

11   consequence of blunt impact trauma, develop after the rupture of

12   blood vessels due to compressive or shearing forces imposed on the

13   body. Bruises are characterized as either subcutaneous or

14   intracutaneous, depending on the tissue layer that is affected. See

15   Bohnert, et al., Spectrophotometric Evaluation of the Colour of Intra-

16   and Subcutaneous Bruises, *Int'l Journal of Legal Medicine 113(6): 343-*

17   *8* (2000). A subcutaneous bruise appears at the site of impact or

18   indirectly by local expansion or shifting of a hemorrhage. After a time

19   interval of hours to days, hemorrhages that are originally localized

20   deep in the tissue layers can extend toward the surface of the skin.

21   The bruise can change color over the course of time from blue to

22   green to yellow during the passing days as a result of the breakdown

23   and diffusion of hemoglobin. When the skin is forced by the

24   application of pressure into channel or profile, the blood is forced into

25   those sections of skin not exposed to the pressure, with hemorrhages

1   occurring as a result of vascular ruptures in the dermis. There have

2   been many studies on how to date bruising and how to distinguish

3   abusive bruising from accidental bruising. See for example, Bariciak,

4   et al., Dating Bruises in Children: an Assessment of Physician

5   Accuracy, *Pediatrics 112(4), 804-7* (2003); Dunstan, et al., A Scoring

6   System for Bruise Patterns: A Tool for Identifying Abuse", *Archives of*

7   *Disease in Childhood 86(5): 330*-33 (2002) and Carpenter, The

8   Prevalence and distribution of Bruising in Babies, *Archives of Disease*

9   *in Childhood 80: 363-66* (1999). The color impression of a bruise, its

10 spectral signature and the extent of hemoglobin degradation are all

11 indicators of bruise age. Although a few recent studies of

12 spectrometric assessment of skin have been undertaken to diagnose

13 various skin diseases, we are aware of no studies relating to

14 spectrometric assessment of skin to assess bruise condition and age.

15 Assessments are routinely made by physicians without evidence-

16 based, scientific, support and there is currently no objective standard

17 or device for assessing bruises in mammals, especially humans.

18   Accordingly, there is also a compelling need in the art for a non-

19 invasive device and method to accurately age and assess the condition

20 of bruised tissue.

21

22 INVENTION SUMMARY

23   In one aspect, the invention provides a non-invasive

24 spectrometric device and method for assessing or detecting

25 hemoglobin concentration in mammalian tissues. More specifically,

1   the invention provides a non-invasive spectrometric device and

2   method for assessing or detecting hemoglobin concentration in

3   dermal and epidermal tissues of the skin in mammals. The device can

4   be used to detect hemoglobin concentration in an area of the skin that

5   has been subjected to bruising, in the palpebral conjunctiva area of

6   the eye socket, in the earlobe or in any other tissue surface.

7   Spectrometers are well know in the art. In operation, light

8   energy from a light source enters the spectrometer via an entrance slit,

9   passes through an objective lens, a diffraction grating and an exit slit.

10   The diffraction grating diffracts the light into its component

11   wavelengths and the wavelengths then strikes a detector that

12   generates a voltage in proportion to the intensity of the light hitting it.

13   The voltage drives a read-out device designed to provide the data on

14   the light's intensity. In early spectrometers, only one wavelength

15   could be detected and its intensity measured at a time. More recently,

16   the exit slit and detector have been replaced by an array of charge

17   coupled devices (CCDs), which has enabled measurement of more than

18   one wavelength at a time. (The number of wavelengths that can be

19   simultaneously measured is determined by the number of elements in

20   the CCD array.) The array generates an output that is used to

21   reconstruct the intensity of the light striking each element of the array.

22   This output is sent to a output device such as a monitor, a laptop

23   computer, a PDA (portable digital assistant) device, a printer or the

24   like.

1   In the spectrometric device of this invention the objective lens

2   and diffraction grating are replaced with a spectral imaging apparatus

3   based on electrically switchable color filter technology. The

4   spectrometric device of the invention comprises wavelength filter

5   means as the spectral imaging apparatus for transmitting or reflecting

6   wavelengths of light, light intensity sensor means arranged and

7   disposed to measure the intensity of the wavelengths transmitted or

8   reflected by the wavelength filter means and generate an electrical

9   signal from the wavelengths transmitted or reflected, output

10   processing means connected to the light intensity sensor means to

11   receive and process the output from the light intensity sensor means,

12   and display means connected to the output processing means to

13   display the output.

14   In one aspect, the light intensity sensor means is arranged and

15   disposed in stacked relation to the wavelength filter means such that

16   wavelengths of light are transmitted through the wavelength filter

17   means into the light intensity sensor means. In another aspect, the

18   light intensity sensor means is arranged and disposed in angular

19   relation to the wavelength filter means such that wavelengths of light

20   are reflected from the wavelength filter means into the light intensity

21   sensor means. In both of these aspects the light intensity sensor

22   means may be provided by an array of charged coupled devices (CCD)

23   or by a photodiode. The currently preferred embodiment employs a

24   CCD array.

1   The wavelength filter means comprises at least one pair of

2   planer substrates in parallel-opposed relation, at least one layer of

3   light-wavelength modulating material disposed between the pair of

4   planer substrates to achieve spectral coverage in the visible light

5   spectrum, and a power source in power-providing communication with

6   the substrate. The substrates will typically be composed of ITO-

7   coated glass or plastic such that electricity may be employed as the

8   source of power, but in one aspect of the invention described in detail

9   below, electrically conducting substrates are unnecessary because the

10   source of power is thermal. Three different types of known light-

11   wavelength modulating materials may be employed in the wavelength

12   filter means: deformed helix ferroelectric liquid crystals, holographic

13   polymer dispersed liquid crystals, and cholesteric liquid crystals.

14   The light-wavelength modulating material, in one aspect,

15   comprises deformed helix ferroelectric liquid crystals (DH-FLC),

16   electrically tuned to exhibit pre-determined wavelength selection

17   properties. By "electrically tuned" we mean that when a voltage is

18   applied across the DH-FLC, the pitch of molecules elongates, which

19   correspondingly lengthens the wavelength of light exhibited. As in

20   understood in the art, the voltage applied to DH-FLC crystals varies

21   the pitch, which lengthens the wavelength of light transmitted or

22   reflected. Due to this fact, varying voltages can be applied to the DH-

23   FLC materials to set the materials to transmit or reflect at pre-

24   determined wavelengths. Typically DH-FLC have been employed in

25   display applications. In such applications, parallel boundary

1   conditions are employed. In the DH–FLC of this inventions, the

2   molecules in the layers of the DH–FLC employed are aligned

3   perpendicular to the surfaces of the planer substrates, i.e.

4   homeotropic alignment. This modification achieves the reflective

5   capacity of the material.

6   The power source employed to modulate the DH–FLC can be

7   either electrical power or thermal power. For thermal power

8   applications, a transparent resistive heater or other thermal power

9   source is positioned on the planer, exterior, surface of one of the

10 substrates, which are not ITO coated. For electrical power

11 applications, the electrical power source is connected to the

12 conducting elements, the ITO coating, of the substrate to create an in–

13 plane electric field using well-know techniques in the art.

14   In another aspect, the spectrometric device of the invention

15 includes light-wavelength modulating material composed of

16 holographic polymer dispersed liquid crystals (H–PDLC) disposed

17 between electrically conducting substrates. In this aspect, the light

18 wavelength modulating material and electrically conducting substrates

19 are arranged in a stack. The stack is composed of a plurality of layers

20 of H–PDLC arranged in alternating, superposed, relation to a plurality

21 of substrate layers. The number of substrate layers equals the number

22 of layers of H–PDLC, plus one. In other words, the wavelength

23 modulating material includes alternating layers of, from bottom to top,

24 substrate and H–PDLC in a stack with the top layer being a layer of the

25 substrate. Each side of the substrate layer adjacent to H–PDLC will

1   have an electrical conducting coating, for example indium–tin–oxide

2   (ITO) in order to complete the circuit. Consequently, the top and

3   bottom layers of substrate may have an electrical conducting coating

4   on only the side, the side disposed interiorly and adjacent to the H–

5   PDLC. The stack may be composed of as many alternating layers of

6   electrically conducting substrate and H–PDLC as is desired but

7   preferably the stack will be composed of between two and ten layers of

8   H–PDLC (and therefore between three and eleven layers of substrate).

9   In one embodiment of this aspect of the invention, the stack is

10   composed of one layer of H–PDLC sandwiched between two layers of

11   electrically conducting substrate. In this aspect, there exists in the H–

12   PDLC film a variable index of refraction of the liquid crystal, which is

13   different from the index of refraction of the polymer. This variable

14   index of refraction permits continuous modification of the reflection or

15   transmission peak, thereby eliminating the need for multiple

16   "gratings", each providing reflection or transmission at a single peak.

17   These variable refraction index H–PDLC and their operation are

18   described in detail in United States Patent Publication No.

19   2002/0130988 herein incorporated by reference.

20   In an alternate embodiment of the invention, the light–

21   wavelength modulating material is composed of cholesteric liquid

22   crystals (CLC) disposed between electrically conducting substrates. In

23   this embodiment the CLC may also be composed a plurality of CLC

24   layers arranged in alternating, superposed, relation to a plurality of

25   substrate layer. In this case, the stack will have a number of substrate

1   layers one greater than the number of CLC layers and the power

2   source will produce electrical energy perpendicular to the pitch axis of

3   the CLC layers.

4   The CLC layers have the capacity to reflect light of different,

5   per-determined wavelengths, but because they are inherently reflect

6   light in a right or left handed manner, the maximum efficiency will be

7   only 50%.   Consequently, to increase the efficiency, the device may

8   further include a passive optical element such as a quarter-wave plate

9   disposed in parallel relation between two reflective CLC of opposite-

10   handedness.

11   In another aspect, one CLC layer may be interposed between two

12   electrically conducting substrate layers. In this aspect, there exists in

13   the CLC film a variable index of refraction of the liquid crystal, which is

14   different from the index of refraction of the polymer. Like the variable

15   refraction index H-PDLC, the variable index of refraction in the CLC

16   permits continuous modification of the reflection or transmission

17   peak, thereby eliminating the need for multiple "gratings", each

18   providing reflection or transmission at a single peak.

19   The output processing means connected to the light intensity

20   sensor means to receive and process the output from the light

21   intensity sensor means can be any of the well-known output

22   processing means employed in spectrometers. Likewise, the display

23   means connected to the output processing means to display the

24   output can be configured using well-known techniques in the art to

25   display indicia of the estimated level of hemoglobin detected.

1   In the operation of the device of the invention, light is projected

2   from the area of epidermal tissue of interest into the device and is

3   then filtered by the wavelength filter means and detected by the light

4   sensor means of the device, the latter of which generates an electrical

5   signal from the wavelengths transmitted or reflected and transmits

6   that signal to the output processing means, which processes the

7   output and transmits it to a display readable by a physician or other

8   health care professional. The basics of how spectrometers and other

9   spectroscopic tools (such as, for example, spectrophotometers) work

10   is well known in the art and succinctly described in Steven L. Brown,

11   "Laboratory Techniques for General Chemistry, Ch. 5, Spectroscopy",

12   2002, Hayden–McNeil Publishing, Plymouth, Michigan.

13   The invention also includes a method of detecting or assessing

14   the concentration of hemoglobin in a mammalian subject suspected of

15   having an abnormal hemoglobin concentration. The method comprises

16   the steps of (a) exposing an area of tissue of a mammalian subject

17   suspected of having an abnormal hemoglobin concentration to a

18   spectrometer of the invention to receive and analyze light reflected

19   from the area of tissue; (b) reading the output from the spectrometer

20   indicating the hemoglobin concentration in the area of tissue exposed

21   to the spectrometer; and (c) comparing the hemoglobin concentration

22   of the output to the hemoglobin concentration in a control standard

23   for a normal epidermal tissue specimen.

24

25   DESCRIPTION OF THE DRAWINGS

13

1   Fig. 1 is an illustration of a H-DPLC containing device. In (a) the

2   prior art panel is illustrated in its voltage-off and voltage applied

3   positions. In (b) and (c) two embodiments of the device of the

4   invention are illustrated in which only one layer of H-DPLC is

5   employed.

6   Fig. 2 is a graphic representation of the transmission results (a)

7   and the reflection results (b) for the stack of five H-DPLC layers

8   described in detail below.

9   Fig. 3 illustrates the mode of operation of a prior art CLC panel

10   (a) in planar (left), focal conic (middle) and homeotropic (right) states.

11   In (b) an embodiment of the invention composed of a stack of three

12   CLC panels is illustrated. In (c) an embodiment of the invention

13   composed of one CLC in IPS mode is illustrated.

14   Fig. 4 is a graphic representation of the transmission results (a)

15   and the reflection results (b) for a CLC device composed of three panel

16   pairs to reflect read, green and blue as described in detail below.

17   Results are shown in (c) for a single panel CLC IPS device that nearly

18   covers the entire spectral range as described in detail below.

19   Fig. 5 illustrates the device of the invention comprising DH-FLC

20   crystals subject to in-plane switching to produce a red-shift.

21   Fig. 6 is a graphic representation of the transmission results (a)

22   and reflection results (b) as temperature varies in the DH-FLC

23   containing device of the invention.

24

25   DETAILED DESCRIPTION

1   In the spectrometric device of this invention the objective lens

2   and diffraction grating are replaced with a spectral imaging apparatus

3   based on electrically switchable color filter technology. The

4   spectrometric device of the invention comprises wavelength filter

5   means as the spectral imaging apparatus for transmitting or reflecting

6   wavelengths of light, light intensity sensor means arranged and

7   disposed to measure the intensity of the wavelengths transmitted or

8   reflected by the wavelength filter means and generate an electrical

9   signal from the wavelengths transmitted or reflected, output

10   processing means connected to the light intensity sensor means to

11   receive and process the output from the light intensity sensor means,

12   and display means connected to the output processing means to

13   display the output. The light intensity sensor means may take the

14   form of an array of charge coupled devices (CCDs) or a photodiode.

15   The output processing means and display means are both well-

16   recognized elements of spectrometric devices and need not be

17   described in detail here as the skilled artisan would be able without

18   undue experimentation to arrange, connect and incorporated these

19   elements. Any of the well-known output processing means and

20   display means known in the art may be used.

21   In one aspect, the light intensity sensor means is arranged and

22   disposed in stacked relation to the wavelength filter means such that

23   wavelengths of light are transmitted through the wavelength filter

24   means into the light intensity sensor means. In another aspect, the

25   light intensity sensor means is arranged and disposed in angular

1   relation to the wavelength filter means such that wavelengths of light

2   are reflected from the wavelength filter means into the light intensity

3   sensor means.

4   The wavelength filter means comprises at least one pair of

5   planer substrates in parallel-opposed relation, at least one layer of

6   light-wavelength modulating material disposed between the pair of

7   planer substrates to achieve spectral coverage in the visible light

8   spectrum, and a power source in power-providing communication with

9   the substrate. The substrates will typically be composed of ITO-

10   coated glass or plastic such that electricity may be employed as the

11   source of power, but in one aspect of the invention described in detail

12   below, electrically conducting substrates are unnecessary because the

13   source of power is thermal. Three different types of known light-

14   wavelength modulating materials may be employed in the wavelength

15   filter means: holographic polymer dispersed liquid crystals (H-PDLC),

16   cholesteric liquid crystals (CLC), and deformed helix ferroelectric liquid

17   crystals (DH-FLC). These types of liquid crystals are well-known in the

18   art. Their use, including the modifications necessary or desirable to

19   employ them in the spectrometric device of the invention, is described

20   in detail below.

21   A.   H-PDLC containing devices

22   Holographic polymer dispersed liquid crystals are created by a

23   simple one-step fabrication process in which a homogeneous mixture

24   of photosensitive propolymer and nematic liquid crystal is exposed to

25   an interference pattern process following the method disclosed in

1   Bowley and Crawford, "Diffusion Kinetics of Formation of Holographic

2   Polymer Dispersed Liquid Crystal Display Materials", 2000, *Applied*

3   *Physics Letters 76.* In the bright regions of the interference pattern

4   the polymerization occurs more rapidly that in the dark regions,

5   forcing the non-reactive liquid crystal out of the bright regions and

6   into the dark regions. This diffusion process creates a stratified

7   material composed of liquid crystal droplets and polymer rich layers

8   that is locked-in by the photo-polymerization process. The grating

9   pitch is given by $\Lambda = \lambda_{f/}/2 <n> \sin \theta$, where $\lambda_{f/}$ is the wavelength of the

10   exposing laser beams, $<n>$ is the average index of refraction of the

11   liquid crystal and polymer mixture , and 2θ is the angle between the

12   exposure beams inside the sample. Since the liquid crystal typically

13   has an average index of refraction that is larger than that of the

14   polymer, a spatial perturbation in the index of refraction exists.

15   The principle is illustrated in Fig. 1(a). The H-PDLC includes

16   liquid crystal and matrix polymer layers (20) which form a reflection

17   grating capable of reflecting a wavelength of light disposed between a

18   pair or more than one pair of electrically conducting substrates (10),

19   which may be formed from indium-tin-oxide (ITO)-coated glass or

20   plastic. See for example, PCT Patent Publication WO 01/20406

21   published 22 March 2001, which discloses a multicolored reflection

22   liquid crystal display device in which the liquid crystal film is capable

23   of reflecting two different wavelengths of light. Each electrically

24   conducting substrate layer (10) is connected with a means for

1   providing electrical energy through the electrodes of the conductant

2   (30) and into the H-PDLC (20).

3   In the absence of an applied voltage, a refractive index

4   modulation exists between the liquid crystal rich planes (shown as

5   droplets) and the pure polymer planes of the H-PDLCs. The average

6   index of refraction of the liquid crystal rich layers, n_{LC}, is some

7   combination of the ordinary, n_o, and the extraordinary, n_e, index of

8   refraction of the liquid crystal, which is estimated as $n_{LC}^2 \approx (n_e^2 +$

9    $2n_o^2)/3$. When the material is illuminated with a broadband white-

10   light source, a narrow reflection band is rejected with reflectives

11   greater than 50% and peak widths in the 15-30 nm range depending

12   on the birefringence of the liquid crystal, index of refraction of the

13   polymer, and sample thickness. Since liquid crystal molecules possess

14   a positive dielectric anisotropy they align parallel to the applied

15   electric field when an external voltage (40) is applied. In the aligned

16   state, the ordinary refractive index of the liquid crystal matches that of

17   the polymer and the index modulation vanishes. The H-PDLC (20)

18   becomes transparent to all wavelengths, as shown in Fig. 1(a), right

19   panel. Switching voltages in the range of 50-100 volts are needed,

20   since the liquid crystal is highly constricted by the holographic planes

21   of dimensions 170-200 nm for visible reflections; however, the

22   response times can be very fast, in some cases, less than 100 μ

23   seconds.

24   In one embodiment of the current invention, these HPDLCs are

25   employed as a spectrometric device. This embodiment is illustrated in

1   Fig 3(b), in which the spectrometric device comprises a plurality of

2   planer H-PDLC film layers disposed in alternating, stacking relation

3   with a plurality of planer ITO-coated substrate layers. The H-PDLC

4   stratified films are sandwiched between the ITO coated glass

5   substrates and maintained at a distance of between about 2 to about

6   30 micronmeters. Between 2 and 20 H-PDLC film layers, and therefore

7   between 3 and 21 substrate layers may be employed. Preferably,

8   between 2 and 10 layers of H-PDLC and therefore between 3 and 11

9   substrate layers may be employed. Electrical leads 30 are then

10   connected to the edges of each of the planer ITO glass substrates so

11   the H-PDLC material can be exposed to an applied voltage. When a

12   voltage is applied, an electric field is created within the material and

13   the H-PDLCs can be tuned to a transparent state. By using multiple H-

14   PDLC layers, various wavelengths can be allowed to pass through the

15   stack by applying different voltages to the different substrate layers.

16   In Fig. 1(b), the stack is shown with broad band incident white light,

17   $\Delta\lambda_w$, and three reflection bands λ_{B1}, λ_{B2}, λ_{B3}, whose peak wavelength is

18   dictated by Bragg's law, $\lambda_B = 2d<n>$ for normally incident light, where

19   d is the thickness of the holographid plane. In the embodiment

20   illustrated in Fig. 3(b), a stack of three H-PDLC layers is shown but the

21   device may be constructed with more or less than three layers to

22   generate a number of reflection bands corresponding to the number of

23   H-PDLC layers in the stack.

24   In another embodiment, the stack is composed of five H-PDLC

25   film layers interspersed between planer ITO-coated substrates instead

1   of three layers as described above. Fig. 2 is a graphic representation

2   of data for such a stack in transmission, Fig. 2(a) and in reflection, Fig.

3   2(b). In reflection (Fig. 2(b)), the five-layered H-PDLC stack exhibits

4   between 30-40% reflectance in the wavelength range between about

5   600 and 760 λ [nm].

6   Referring again to Fig. 1, parts (c) and (d) illustrate two alternate

7   embodiments of this aspect of the inventions. In the aspect illustrated

8   in (c), only one H-PDLC film is needed and employed because a spatial

9   gradient has been created in the holographic plane sizes from one

10   edge of the sample to the other. The H-PDLC sample can then act as a

11   wavelength modulating material for multiple wavelengths. In order to

12   selected different wavelengths, the ITO coating can be pixilated so that

13   the various wavelengths can be electrically addressed independently.

14   In the alternate embodiment shown in (d), only one H-PDLC film

15   is needed and employed because there exists in the H-PDLC film a

16   variable index of refraction of the liquid crystal, which is different from

17   the polymer. In this way, as the electric field is applied to the two

18   substrates, and the index of refraction changes with respect to the

19   index of the polymer enabling the H-PDLC to be electrically addressed

20   to a pre-determined wavelength. This alternate embodiment is

21   described in detail in PCT Patent Publication WO 01/20406 published

22   22 March 2001, which is herein incorporated by reference.

23   All of these above embodiments of H-PDLC can be used in the

24   non-invasive, spectrometric device of the invention to assess

25   hemoglobin concentration in the blood of mammalian tissues.

1

2   B.   CLC containing devices

3   Cholesteric liquid crystals (CLC) are also known in the art. CLC

4   exhibit long-range, orientational order analogous to conventional

5   nematic liquid crystals, except that the molecules are chiral. See

6   Blinoff and Chigrinov, Electro-Optic Effects in Liquid Crystals, Springer,

7   New York, (1994). Consequently, the structure acquires a

8   spontaneous right-handed or left-handed twist about a helical axis

9   normal to the average direction of the liquid crystal molecules. The

10   degree of twist of the phase is characterized by the cholesteric pitch,

11   "P". Heretofore, CLC have been used in flat -panel display

12   applications. See Yang, et al., in Liquid Crystals in Complex

13   Geometries Formed by Polymer and Porous Networks, Crawford, GP

14   and Sumer, S, eds., Taylor & Francis, London (1996); Doane, et al.,

15   Cholesteric Liquid Crystals for Flexible Display Applications, John Wiley

16   & Sons, London, (2004). The operation of a CLC device is illustrated in

17   Figure 3(a)left panel. In the zero voltage state illustrated in the left

18   panel, the molecules are aligned in the planar configuration between

19   the substrate layers, and since the structure is periodic, they can

20   reflect a bandwidth centered at λ_B, which is dictated by Bragg's law (λ_B

21   = $<n>P$ for normal incidence). Upon application of an applied voltage

22   ($V_1 \sim 10$-15 volts for a 5 μm sample), a positive dielectric anisotropy

23   material ($\Delta\varepsilon > 0$) transforms to a focal conic state, which is

24   characterized by a random distribution of helical pitches, as shown in

25   Fig. 3(a), middle panel. This state is transparent and remains that way

1   even after the voltage is removed. In other words, this device

2   possesses bi-stable memory since the focal conic state can remain

3   indefinitely even after the field is removed. Upon application of a

4   higher voltage (V_2 ~ 25-30 volts), the material transforms to the

5   hometropic, aligned, state as shown in Fig. 3(a), right panel. When the

6   voltage is abruptly removed, the homeotropic state transforms back to

7   the reflective planar state. Fig. 3(a) right panel. The chiral pitch can be

8   engineered, or set, by mixing in different concentrations the chiral

9   components to reflect in the ultraviolet, visible and near infrared in

10   accordance with art-recognized tehchniques. The switching time is on

11   the order of 30-50 ms slower, depending on the mode, than other

12   liquid crystal materials.

13   In order for CLC to be used in a non-invasive spectrometer, full

14   spectral coverage in the visible light spectrum is required. This can be

15   achieved by employing a CLC stack, comprising a plurality of layers of

16   cholesteric liquid crystal materials. Fig. 3(b) illustrates a three-stack

17   of CLC panels that reflect red, green and blue. Fig. 4(a) presents the

18   data for this stack in the transmission mode and Fig. 4(b) presents the

19   data for this stack in the reflection mode upon application of the

20   applied voltage. Since CLC are intrinsically right- or left-handed

21   because of their chirality, they can reflect only right-handed or left-

22   handed, circularly polarized, light, ideally with 50% efficiency at the

23   Bragg wavelength. To solve this problem, we disposed and arranged

24   the panels that reflected red, green and blue as panel pairs, each color

25   having a right handed and a left handed panel forming the respective

1   pairs, so that we actually had six panels in the stack, two red, then two

2   green, then two blue. We then integrated a passive optical element

3   between two identically reflecting panels to achieve a much higher

4   efficiency, exceeding 80%, as shown in Fig. 4(a) and (b). In the

5   embodiment illustrated the passive optical element employed was a

6   quarter-wave plate, but the skilled artisan will recognize that any

7   passive optical element could be used. Alternatively, to achieve the

8   same outcome, a left handed panel and a right handed panel with the

9   same λ_B can be stacked.

10   The stacked solution illustrated in Fig. 4(b) was experimentally

11   evaluated and the results are shown in Fig. 5(a) and (b). The full

12   spectral width of the reflection peak in Fig. 4(b) is $\Delta\lambda_{FWHM} > 100nm$.

13   The spectral width is largely dictated by the birefringence of the CLC

14   material, Δn. To decrease the spectral bandwidth, materials with a

15   lower Δn can be employed. For example, for a material with a

16   $\Delta n \sim 0.05$, bandwidths on the order of $\Delta\lambda_{FWHM} \sim 30nm$ for $\lambda_B = 600nm$

17   can be achieved. Because CLC materials do not have the scattering

18   losses observed with H-PDLC materials, numerous panels can be

19   stacked to achieve full spectral coverage in the visible range.

20   A CLC in-plane switching (IPS) mode is shown in Fig. 4(c) in

21   which field direction is parallel to the substrates, orthogonal to how it

22   was applied in Fig. 4(a) and (b). As an in-plane voltage is applied

23   perpendicular to the pitch axis of the CLC, the pitch elongates and the

24   reflection red-shifts. This IPS mode permits the use of one panel to

25   span nearly the entire visible spectral range, as is shown in Fig. 4(c).

1   This mode enable electrical tuning of the reflection band from 450 nm

2   to 700nm. Assuming linearity in the transition region, the

3   tunability/resolution metric is $\Delta V/\Delta\lambda\sim$ 0.15 V/nm for the peak

4   maximum. The downside of this approach is that overall efficiency

5   may be reduced because the electrodes on the surface of the substrate

6   reduce the optical throughput, as CLC materials do not respond above

7   the electrode. By offsetting a pair of transparent conducting

8   electrodes on the top and bottom substrates and by driving them with

9   voltage signals out of phase, this problem is alleviated. In addition,

10   because the switching voltage is higher in the CLC IPS mode as

11   compared to conventional IPS mode, the electrodes must be arranged

12   closer together so that maximum drive voltages do not exceed 40–50

13   volts. The preferred distance between electrodes is around 5 μm, but

14   the skilled artisan will recognize that distance between electrodes can

15   be optimized for various materials without any undue

16   experimentation.

17   C.   DH-FLC

18   The art-known ferroelectric liquid crystal, or chiral smectic C

19   phase (SmC) liquid crystals, consists of layers of molecules. This

20   thickness of the chiral smectic C layers are less than one molecular

21   length. See Yeh and Gu, Optics of Liquid Crystals, John Wiley, New

22   York, (1999). As a result, the molecules must tilt at an angle with

23   respect to the layer normal. Because the tilt angle is fixed, the

24   molecular orientation is confined to a cone with a half apex angle of θ.

25   Ferroelectric liquid crystal materials have intrinsic chirality and

1   associated pitch, much like CLC materials, and they have a dipole

2   moment perpendicular to the long molecular axis, rather than parallel

3   to it as in the case of CLCs materials. In ferroelectric switching, the

4   molecules switch on the cone.

5   Art-known, deformed helix ferroelectric liquid crystal materials

6   (DH-FLC) were first used in display applications. See Verhulst, et al., A

7   Wide Viewing Angle Video Display Based on Deformed Helix

8   Ferroelectric LC and Diode Active Matrix, *Proceeding of the*

9   *International Display Research Conference 94: 377-80* (1994). In

10   those applications, parallel boundary conditions were employed, i.e.,

11   the molecules are aligned in parallel to the substrate surfaces In this

12   embodiment of the invention, homeotropic alignment, wherein the

13   molecules are aligned perpendicular to the substrate surfaces, should

14   be employed so that the panel provides a wavelength selection

15   property similar to the CLC panel. Dynamic switching times for panels

16   of DH-FLC materials operated as described above should be less than

17   500 µs.

18   This embodiment is illustrated in Fig. 5. Pitch is deformable

19   using temperature or an in-plane electric field. If an in-plane electric

20   field is employed, the helix deforms or elongates and the reflection

21   red-shifts. If the in-plane switching (IPS) mode described above for

22   CLC materials is employed, the same disadvantages described will

23   result and accordingly, the IPS electrodes should be located closer

24   together to minimize aperture loss. A preferred range is about 5 µm,

25   but the skilled artisan will recognize that distance between electrodes

1   can be optimized for various materials without any undue

2   experimentation. If temperature is employed to accomplish switching,

3   a transparent resistive heater may be incorporated into the device and

4   employed in place of electric power in accordance with well-

5   recognized methods. A DH-FLC panel having homeotropic alignment

6   at the surfaces, i.e., in which the molecules are aligned perpendicular

7   to the plane of the layer was prepared and subjected to temperature

8   increases. The data is presented in Fig. 6(a) and (b) for transmission

9   and reflection, respectively. Since the refractive index of the material

10   was small and the cone angle was around 30 degrees, the sample was

11   tilted with respect to the incident light to increase the index

12   perturbation with respect to the incoming light. One DH-FLC panel

13   can cover the entire visible spectral range, as is illustrated in Fig. 6(c).

14   Assuming linearity in the transition region if Fig. 6(c), the

15   tenability/resolution metric is $\Delta V / \Delta \lambda \sim 0.12$ °/nm.

16   The DH-FLC panels of the invention may be switched either

17   electrically or thermally. Electrical switching is currently the preferred

18   mode. Like the CLC-containing devices of the invention , electrical

19   switching may be accomplished by advantageous employment of the

20   herein disclosed IPS mode, in which the field direction is parallel to the

21   substrates. Thermal switching can be accomplished by employing a

22   transparent resistive heater, which is connected to a power supply

23   (typically a current source) employing methods and materials well-

24   know in the art.

1   Other embodiments are within the scope and spirit of the

2   claims. Certain elements and functions of the invention described

3   above can be implemented using software, hardware, firmware,

4   hardwiring, or any combinations of these in art–recognized ways.

5   Features, elements and means of the invention implementing various

6   functions may be physically located at various positions rather than in

7   a single location or apparatus.

8   All references cited in this document are hereby incorporated by

9   reference herein for the substance of their disclosure.

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